# Neonatal Management During the Coronavirus Disease (COVID-19) Outbreak: The Chinese Experience

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## BACKGROUND

Novel coronavirus infection is a disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and was named COVID-19 by the World Health Organization on January 7, 2020. In early December 2019, a number of pneumonia cases of unknown origin emerged in Wuhan, Hubei province, China. (1)(2) The disease then spread rapidly throughout China and has now become a global pandemic. As of March 23, 2020, more than 340,000 cases have been reported in more than 150 countries. Because the disease is primarily an airborne respiratory infection and is documented to have a strong human-to-human transmission, the pediatric and neonatal populations are vulnerable to this disease. However, the incidence and clinical presentations of pediatric COVID-19 infections are varied and differ from those found in adult patients. The atypical clinical presentations and 2 potential modes of transmission in neonates (ie, maternal-fetal or maternal-neonatal) have led to diagnostic and management challenges. In this perspective, we would like to share some published information from Chinese pediatric and neonatal societies about their approach to handling the 2019-2020 COVID-19 outbreak in China.

## THE INCIDENCE AND CLINICAL CHARACTERISTICS OF COVID-19 IN PEDIATRIC AND NEONATAL POPULATIONS

Since the COVID-19 outbreak in December 2019, more than 81,000 confirmed cases have been reported in China (as of March 23, 2020). Most of these cases occurred between late January and early February 2020. The diagnosis of COVID-19 is based on the epidemiologic history of contact with an infected person, typical clinical features such as fever and respiratory distress, and a positive real-time polymerase chain reaction to the SARS-CoV-2 RNA test. The nucleic test is considered the gold standard for confirmation.

As of February 8, 2020, 731 confirmed pediatric cases were reported in China, mainly from Wuhan city. (3) Relative to the total number of cases (n=34,664) reported in China, on February 8, 2020, the pediatric COVID-19 population accounted for 2.1% of all confirmed cases. In a more recent summary reporting 44,672 confirmed cases from the Chinese Center for Disease Control and Prevention, the percentage of pediatric infected patients was 1% of the total infected cases in children younger than 10 years (n=416) and 1% of the total infected cases in children between 10 and 19 years of age (n=549). (4) However, the incidence reported in a different city in China varied. Bi et al reported that in the city of Shenzhen, pediatric patients up to 19 years of age accounted for 8.2% of

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all cases. (5) Based on a recent census in Shenzhen, the percentage of the population that is below 19 years of age is 17%, suggesting that the affected number of pediatric cases of 8.2% should not be considered very low. (5) However, we do know that the severity of symptoms in pediatric patients with COVID-19 has been generally mild. Dong et al reported 731 confirmed pediatric cases and found that 94 patients (12.9%) were asymptomatic, 315 (43%) had mild symptoms, 300 (41%) had moderate symptoms, and 18 (2.5%) had severe symptoms. Only 3 (0.2%) of 731 pediatric patients were critically ill. (3)

Thus far, only a limited number of confirmed neonatal cases have been reported in China. The possibility of maternal-to-fetal vertical transmission is a major concern among neonatal and perinatal societies. Direct evidence for vertical transmission of SARS-CoV-2 is lacking. Chen et al retrospectively reviewed the clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in 9 pregnant women in Wuhan city. (6) In this group, maternal clinical records, chest computed tomography (CT) scans, and laboratory-confirmed COVID-19 pneumonia (ie, using throat swab samples) were all consistent with the SARS-CoV-2 infection. All 9 patients had cesarean deliveries in their third trimester (between 36 0/7 and 39 4/7 weeks' gestation). Nine live births were recorded. None of the newborns had perinatal depression. Amniotic fluid, cord blood, neonatal nasopharyngeal or throat swab, and breast milk samples for SARS-CoV-2 RNA from 6 mother-neonate dyads were tested, and all samples tested negative for the virus. (6) These results are similar to those found in the SARS-CoV-1 infection that occurred 17 years ago. (7) The interpretation of the findings from this recent small group of cases suggests that there is currently no evidence for intrauterine infection caused by vertical transmission in women who develop COVID-19 pneumonia in late pregnancy. Nonetheless, with the small sample size observed, the possibility of vertical transmission cannot be ruled out completely. In a report by Zhu et al, 10 pregnant women who tested positive for COVID-19 and delivered neonates (gestational age in weeks: 31, 31, 33 6/7, 34 2/7, 34 5/7, 34 6/7, 37 [large for gestational age], 38 4/7 [small for gestational age], 39, and 39 [large for gestational age]) were all negative for the SARS-CoV-2 RNA test. (8) Not surprisingly, it is difficult to distinguish potential COVID-19 symptoms from the common symptoms of mild respiratory distress syndrome, transient tachypnea of the newborn, and sepsis. In 1 particular neonate in this cohort (38 4/7 weeks, 2,450 g, small for gestational age), the chest CT scan showed a ground glass opacity pattern, which is the typical CT finding in adult patients with COVID-19. This neonate had mild respiratory distress but did not require mechanical ventilation, and the possibility of an infection with SARS-CoV-2 could not be ruled out. As such, the National Health Commission of China recently proposed strengthening family counseling, screening, and follow-up of infants born to COVID-19–positive women. There is still uncertainty about whether the duration of maternal viral infection and the birth gestational age affects the rate of positive test results in the neonate.

The number of confirmed neonatal cases is limited. So far, 6 cases have been reported in China. (9)(10) One report of 5 cases was published in a Chinese journal and another case was reported by the local news media. Of these 6 patients, 1 presented with symptoms at 30 hours of age and tested positive for SARS-CoV-2 RNA at 36 hours after birth. However, whether this case represented a vertical transmission from the mother remains to be confirmed. (10) All 6 reported cases presented with nonspecific clinical symptoms or signs that did not require intubation and were discharged after complete recovery (Table).

## NEONATAL HEALTH CARE SOCIETY RESPONSE TO THE OUTBREAK OF COVID-19

During the COVID-19 outbreak and mass quarantine implementation in late January and February 2020, most elective surgical procedures were postponed. Nonemergent hospital visits were decreased and the general medical ward capacity was reduced to at least 50%. This allowed hospitals to mobilize the space and manpower to concentrate on patients with COVID-19. Patients with COVID-19 were treated in special hospitals, designated as level III, which contain "negative pressure" wards (typically in isolated buildings) reserved for severe infectious disease admissions. When possible, infected or suspected neonates were admitted to this ward and the NICU team would be responsible for the infant's care; these neonates were also placed in incubators to reduce the potential of airborne transmission between patients and health care personnel.

For the COVID-19 response, perinatal and neonatal hospital providers relied on recent published consensus guidelines that were developed and published by Chinese neonatal and perinatal societies and lessons that were learned during the experience of the 2003 SARS-CoV outbreak. (11) The neonatal guideline focuses on perinatal infection prevention, high-risk neonatal transport, staff allocation and training, special equipment for transport, and intensive care preparation. The recommendations stress the importance of prevention and control of hospital infections. Family-integrated care and parental visits, including breastfeeding visits, are suspended during the neonate's hospitalization. In addition to the standardized personal protective clothing and gloves, some specialized equipment or devices, such as

TABLE. **Clinical Characteristics of 6 Covid-19 Neonatal Cases in China**

| PATIENT/ CITY | AGE | CLINICAL PRESENTATIONS[a] | MOTHER SARS-COV-2RNA RESULT | HEST RADIOGRAPH/ CT SCAN | PHARYNGEAL/RECTAL SWAB FOR SARS-COV-2 | GESTATION | OUTCOME |
|---|---|---|---|---|---|---|---|
| 1/Wuhan[b,c] | 30 h | Poor feeding, fever, vomiting | + | −/− | +/− | Term | Full recovery |
| 2/Wuhan[b] | 18 d | Vomiting, lethargy | −(with typical clinical and CT findings) | −/− | +/− | Term | Full recovery |
| 3/Wuhan[b] | 12 d | Sneezing (mild), vomiting, diarrhea | + | −/nonspecific lung markings | +/+ | Term | Full recovery |
| 4/Wuhan[b] | 3 d | Fever, lethargy | + | −/nonspecific lung markings | +/− | Term | Full recovery |
| 5/Wuhan[b] | 36 h | Poor feeding, lethargy | + | Pneumonia/ GGO | +/− | Term | Full recovery |
| 6/Xinyang[d] | 5 d | Fever | + | −/not done | +/not done | Term | Full recovery |

*CT=computed tomography; GGO=ground glass opacity; plus (+) sign=positive; minus (−) sign=negative.*

[a] *None of the patients required intubation.*

[b] *From Xiaoyuan et al. (9)*

[c] *From Wang et al. (10)*

[d] *From news media of hospital report.*

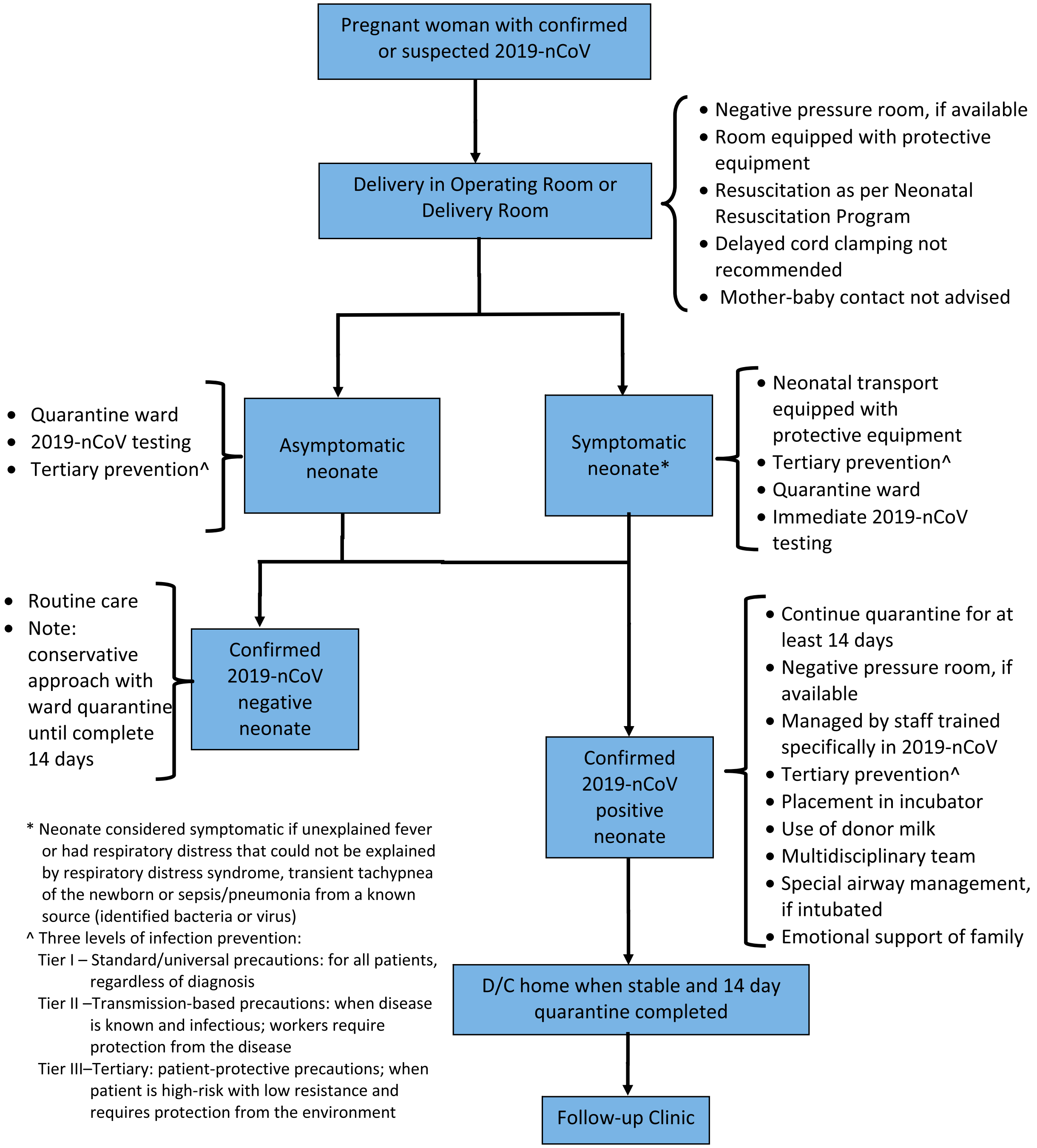
ventilator exhaled port viral filters, suction catheters with a sealed sheath, and disposable ventilator tubing systems, are used in the specialized ward or during transport by ambulance. Staff are trained in infectious disease control, prevention, and the use and sequence of protective clothing, and practiced by all staff taking care of patients with COVID-19. The handling and disposal of dirty diapers is extremely important. It was recently reported that children with COVID-19 have prolonged fecal viral shedding for several weeks after clinical recovery. (12) It is still not known whether this viral shedding can lead to transmission of disease. Proper handling of diapers with stool or other secretions (especially respiratory) is potentially an important measure for decreasing the possibility of disease spread both within the unit and after discharge. It is currently unknown whether a bath would alter the risk of potential transmission.

This management approach for neonates born to women with confirmed or suspected COVID-19 was based on Chinese consensus and was established using the current literature on this disease, government recommendations, and the experience from the SARS-CoV epidemic of 2003. (11) Although it is largely not evidence-based, these recommendations are widely practiced now in China for the care of neonates at risk of contracting COVID-19. The consensus flowsheet on neonatal COVID-19 management is summarized in the Figure. (13)

## STRATEGIES FOR NEONATAL OUTPATIENT FOLLOW-UP DURING THE COVID-19 EPIDEMIC

During rigorous quarantine in early February 2020, the National Health Commission of China recommended postponing the routine follow-up hospital visits of newborns. As a result, neonatal health surveillance became challenging, especially for infants at risk for indirect hyperbilirubinemia. The following is an example of how we follow neonates for jaundice during the 2020 epidemic.

To avoid frequent outpatient visits and reduce unnecessary readmissions during the COVID-19 epidemic, we launched a novel online follow-up program in February and March of 2020. (14) Before discharge, every parent is informed of the potential harm of indirect hyperbilirubinemia, the importance of bilirubin monitoring, the availability of online resources, and methods for assessing a newborn infant's condition. In addition, families are provided with detailed information about COVID-19 and prevention strategies. We use a smartphone application (App) (Biliscan, available in Asia, Europe, and Africa) to monitor the transcutaneous bilirubin (TCB) levels of discharged patients. (15)(16) Prior to discharge, parents download and install the App on their smartphone and practice using the software under the direction of medical staff. The parents receive a color calibration card for use at home. To use


Pregnant woman with confirmed or suspected 2019-nCoV
Delivery in Operating Room or Delivery Room
• Negative pressure room, if available
• Room equipped with protective equipment
• Resuscitation as per Neonatal Resuscitation Program
• Delayed cord clamping not recommended
• Mother-baby contact not advised
• Quarantine ward
• 2019-nCoV testing
• Tertiary prevention^
Asymptomatic neonate
Symptomatic neonate*
• Neonatal transport equipped with protective equipment
• Tertiary prevention^
• Quarantine ward
• Immediate 2019-nCoV testing
• Routine care
• Note: conservative approach with ward quarantine until complete 14 days
Confirmed 2019-nCoV negative neonate
Confirmed 2019-nCoV positive neonate
• Continue quarantine for at least 14 days
• Negative pressure room, if available
• Managed by staff trained specifically in 2019-nCoV
• Tertiary prevention^
• Placement in incubator
• Use of donor milk
• Multidisciplinary team
• Special airway management, if intubated
• Emotional support of family
D/C home when stable and 14 day quarantine completed
Follow-up Clinic

* Neonate considered symptomatic if unexplained fever or had respiratory distress that could not be explained by respiratory distress syndrome, transient tachypnea of the newborn or sepsis/pneumonia from a known source (identified bacteria or virus)

^ Three levels of infection prevention:

Tier I – Standard/universal precautions: for all patients, regardless of diagnosis

Tier II –Transmission-based precautions: when disease is known and infectious; workers require protection from the disease

Tier III–Tertiary: patient-protective precautions; when patient is high-risk with low resistance and requires protection from the environment

**Figure.** Flow diagram for the perinatal-neonatal management of suspected or confirmed 2019 novel coronavirus infection (2019-nCoV). Adapted with permission from Wang, Shi, Xiao, et al. *Ann Transl Med*. 2020 Feb; 8(3):47. 10.21037/atm.2020.02.20.

this card, parents place the hollow square area of the card on the infant's skin over the sternum. Parents then take a photograph of the card using the smartphone camera. The image data are then transmitted to the cloud for analysis, and the results of the TCB level are provided in seconds.

Before the online follow-up meeting with the pediatric provider, parents are asked to check the TCB level by smartphone as described before, and also complete a questionnaire about their infant's general clinical condition. The timing of this meeting is based on the infant's birth gestational age, days after birth, and the TCB level on the discharge day. The physician then provides advice to the parents and determines the next online visit based on the newborn's clinical scenario and the TCB level. If the App for TCB measurement is not available, parents can assess the degree of jaundice by observation in natural light. If the TCB level is higher than the 95th percentile in the first week after birth, more than 15 mg/dL (256.5 μmol/L) after 7 days of age, or the increment of bilirubin level is above 5 mg/dL (85.5 μmol/L) within 24 hours, the child is seen in an outpatient clinic. For infants with significant hyperbilirubinemia, we recommend hospitalization rather than outpatient daytime phototherapy, because the outpatient environment increases the risk for SARS-CoV-2 infection.

This program has been used for 1 month in a level 3 maternal hospital. To validate the program, neonates who were diagnosed with ABO hemolytic disease and treated at the Women's Hospital of Zhejiang University from January 20, 2020, to February 29, 2020, were followed using the home bilirubin App on the smart phone or TCB monitor (46 cases). These strategies were compared with routine outpatient follow-up during a similar period of 2018 (56 cases). No significant difference was noted between the 2 groups in the rates of readmission (8% vs 7%) and severe indirect hyperbilirubinemia after adjusting for gestational age, birthweight, delivery mode, gender peak bilirubin levels at first admission, and discharge (unpublished data). The authors concluded that the home-based strategy of follow-up is feasible and effective for neonates with ABO hemolysis after discharge during a period of mass quarantine.

## CONCLUSION

The current COVID-19 pandemic has become the most serious public health problem in the world. Children and newborns are not entirely exempt from the epidemic. Although most evidence-based prevention and control data are not fully available, the newly developed prevention and control consensus strategies for newborn COVID-19 are of great significance. We believe that this approach will protect newborns, their families, and health care professionals. Some of the steps of this consensus approach are currently being validated for use in clinical practice.

## American Board of Pediatrics Neonatal-Perinatal Content Specification

- Know the effective techniques for control of healthcare associated infection in the nursery, NICU, and obstetrical unit.

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